A new synthesis of pyrroles fused with polycyclic skeletons

Satoshi Ito, Takashi Murashima and Noboru Ono *

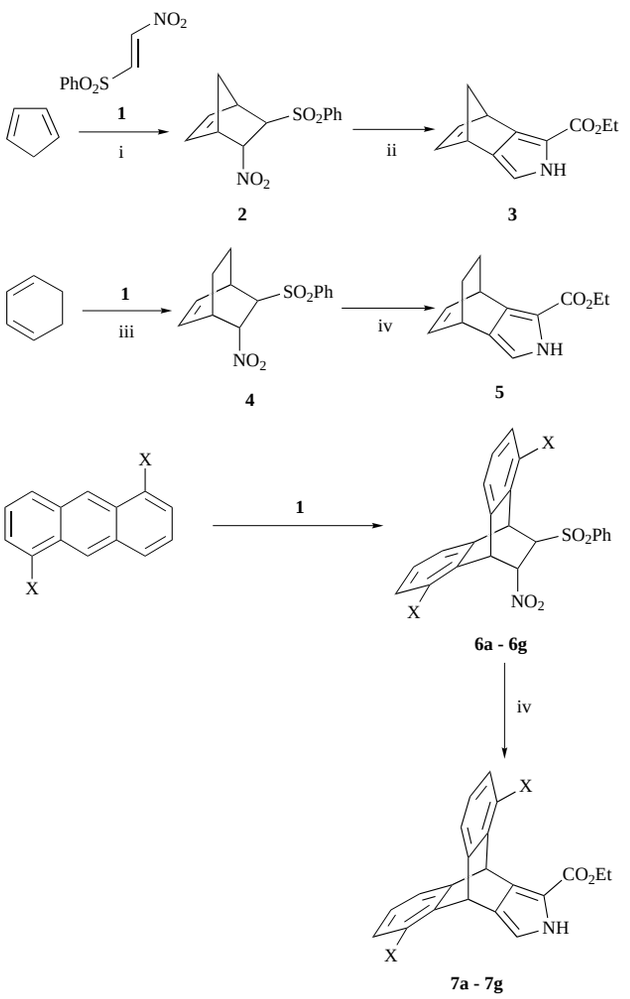
Department of Chemistry, Faculty of Science, Ehime University, Matsuyama 790, Japan

The Diels–Alder reaction of β-sulfonylnitroethylene with cyclopentadiene, cyclohexadiene or substituted anthracenes followed by treatment with ethyl isocyanoacetate in the presence of DBU gives pyrroles fused with bicyclo[2.2.1]heptadiene and bicyclo[2.2.2]octadiene skeletons, or triptycene-types of pyrrole, respectively, which are precursors for novel porphyrins fused with polycyclic skeletons.

β-Substituted pyrroles are important starting materials for the synthesis of new types of porphyrin derivatives with altered or extended chromophores or a variety of substitution patterns.[1] The Barton–Zard pyrrole synthesis based on the reaction of nitroalkenes with ethyl isocyanoacetate provides an ideal method for β-substituted pyrroles which can be used for chemical modification of porphyrins.[2] The pyrroles obtained by this method have an ester function at the 2-position which are converted into 2-hydroxymethylpyrroles by the careful reduction with $LiAlH_4$ (reduction at low temperature for short time) to give porphyrins *via* a biomimetic route.[3] This method has been frequently used for the synthesis of β-substituted porphyrins without meso-substituents, which give suitable models of biological systems.[4] Recently we have successfully extended this pyrrole synthesis to the synthesis of isoindoles using aromatic nitro compounds instead of nitroalkenes.[5] Thus, highly conjugated porphyrins fused with various aromatic rings are now prepared starting from aromatic nitro compounds.[6] The success of pyrrole synthesis of the Barton–Zard method depends on the structures of the nitroalkenes or the nitro aromatics.[7] Our interest has now turned to the preparation of pyrroles and porphyrins fused with polycyclic skeletons, since such compounds provide interesting frameworks for the construction of functionalized materials. Only limited methods for the preparation of such pyrroles are available.[8,9] The known methods suffer from low overall yields and are limited to special substrates. In this paper we report a new general method for the preparation of pyrroles fused with polycyclic skeletons such as **3**, **5** and **7** in Scheme 1, which is based on the Diels–Alder reaction of a nitroacetylene equivalent with dienes and the subsequent Barton–Zard pyrrole synthesis.

Results and discussion

Tetrahydro-2*H*-isoindoles were prepared by the reaction of nitro cycloalkenes with ethyl isocyanoacetate in good yields.[2] So it is expected that pyrroles fused with polycyclic skeletons such as **3**, **5** and **7** can be prepared from polycyclic nitroalkenes by a similar procedure. However, preparation of the requisite polycyclic nitroalkenes is not easy, the best way being, probably, the Diels–Alder reaction of nitroacetylene with cyclopentadiene, cyclohexadiene and substituted anthracenes. However, unsubstituted nitroacetylene is not readily prepared and is too unstable for use in the Diels–Alder reaction. Thus, we planned to use β-sulfonylnitroethylene **1** as a nitroacetylene equivalent for this purpose.[10] β-Nitro sulfones **2**, **4** and **6** prepared by the Diels–Alder reaction of **1** with the corresponding dienes may serve as polycyclic nitroalkenes. Namely, the reaction of them with ethyl isocyanoacetate in the presence of 1,8-diazabicyclo-[5.4.0]undec-7-ene (DBU) may proceed *via* elimination of sulfinic acid, addition of ethyl isocyanoacetate, cyclization and elimination of nitrous acid to give the desired pyrroles.



Scheme 1 *Reagents and conditions*: i, $CHCl_3$, room temp., 12 h; ii, $CNCH_2CO_2Et$, DBU, MeCN, room temp., 24 h; iii, $CHCl_3$, reflux, 8 h; iv, $CNCH_2CO_2Et$, DBU, room temp., 24 h

The Diels–Alder reaction of **1** with cyclopentadiene, cyclohexadiene or unsubstituted anthracene has already been reported, and the adducts **2**, **4** and **6d** were obtained in good yields by the reported procedure.[10] However, the reaction of **1** with substituted anthracenes has not been tried before. It was found that the reaction was much affected by the reaction conditions as summarized in Table 1. High temperature (refluxing in toluene) is required to induce the Diels–Alder reaction of **1** with anthracenes without strong activating groups. For example, whilst **6e** was not formed when the reaction was performed at room temperature, it was obtained in 61% yield when the reaction was performed in refluxing toluene for 5 h. How-

ever, since the yield of **6e** was reduced to 36% if the reaction was continued under the same conditions for 20 h, it is clear that **6e** decomposes at the temperature of refluxing toluene. Such decomposition was serious in the case of Diels–Alder adducts resulting from electron-rich anthracenes. For example, pyrroles **6f** and **6g** were not obtained from reactions conducted in refluxing toluene, black polymers insoluble in most organic solvents, being obtained instead. Although such polymerization may be induced by an electron transfer reaction from an electron-rich anthracene moiety to an electron-deficient β-nitro sulfone function, since the decomposition products were not characterized, the mechanism of this process is not yet clear. However, compounds **6f** and **6g** could be prepared in good yields by reactions carried out at room temperature. Nevertheless, electron-deficient anthracenes (X = CO_2Me, CN) reacted very slowly with **1** to give **6b** (55%) and **6c** (25%). A higher reaction temperature may be required to increase the yield of **6c**. Thus, both electron-rich and -deficient anthracenes give the Diels–Alder adducts **6**, which may be used as nitroalkenes in the Barton–Zard pyrrole synthesis.

The pyrrole synthesis from **2**, **4** and **6** was carried out by a procedure similar to that described in the literature for β-nitro acetates or nitroalkenes.[2] The results are summarized in Table 2. The reaction of **4** and **6** with ethyl isocyanoacetate proceeded nicely in THF using DBU as a base to give the desired pyrroles **5** and **7** in good yields. Substituents X on **6** had no effect on the reaction course to give the pyrroles **7a**–**d**. However, the reaction of **2** with ethyl isocyanoacetate showed rather confusing results. Although a reaction carried out in THF using DBU as a base failed to give the pyrrole **3**, unidentified products being formed instead, use of a phosphazene base (BTPP), which is a stronger non-ionic base than DBU, did give **3** (20%). Since the cyclization of the carbanion formed by the reaction of ethyl isocyanoacetate with nitroalkenes depends on the geometry of the isonitrile function and the carbanion formed, inefficient cyclization of **2** may be due to steric strain generated by the formation of a pyrrole ring which is fused with a norbornadiene skeleton. Surprisingly, this difficulty in pyrrole formation from **2** was simply resolved by using MeCN as a solvent. The effectiveness of MeCN as solvent for the formation of pyrrole **3** is demonstrated by the increased product yield to 61% (see Table 2). Recently, similar dependency of solvents and bases on the reaction pathway of Barton–Zard pyrrole synthesis from aromatic nitro compounds was observed in our laboratory.[11]

Thus, we have established a new method for the preparation of pyrroles fused with polycyclic skeletons such as **3**, **5** and **7** by employing a Diels–Alder reaction of nitro acetylene with cyclic dienes and Barton–Zard pyrrole synthesis. This procedure is attractive for the preparation of pyrroles fused with polycyclic skeletons such as heterocyclic triptycenes and can be extended to a general synthesis of isoindole systems starting from the Diels–Alder reaction of **1** with cyclic and acyclic dienes. Furthermore, since the β-nitro sulfones act as nitroalkene equivalents in the Barton–Zard pyrrole synthesis, this may extend the scope and limitation of this procedure.

The pyrroles **3**, **5** and **7** are important precursors for functionalized polypyrroles or porphyrins. Additional functionality can be readily introduced into such pyrroles (also the final polypyrroles or porphyrins) by using the double bonds or aromatic rings of these pyrroles. Construction of supra molecules by our present strategy using a Diels–Alder reaction for the construction of polycyclic skeletons gives a promising tool for advanced materials. Here, preliminary attempts to convert **3**, **5** and **7** into the corresponding porphyrins were made (Scheme 2). Thus compounds **3**, **5** and **7** were converted into the corresponding porphyrins **9**, **10d** (X = H) and **10e** (X = Me) in 20–30% yield by reduction with $LiAlH_4$ at 0 °C followed by subsequent tetramerization and oxidation with chloranil. The porphyrins **9** and **10e** consisted of a mixture of diastereoisomers which were not separated by column chromatography. Similarly, although **3** could be converted into **8**, the product yield was low; we needed therefore to improve the procedure. Although the porphyrin **8** was not fully characterized by NMR spectroscopy because of traces of impurities, nevertheless absorption spectroscopy suggested its formation. The absorption and NMR spectra (*meso*-H and NH) of these new porphyrins are summarized in Table 3. The absorption maxima for the porphyrins **8** and **10** were shifted to the longer wavelengths, which suggested through-space interaction between π-bonds and porphyrin rings. A more detailed study is, however, necessary to obtain further information on such an interaction. The ^1H NMR spectra of the porphyrins **10d** and **10e** provide important information on their structure. Thus, the *meso* and NH protons appeared at δ 10.5 and −4.95, respectively, values which are either lower or higher than those of ordinary porphyrins: the chemical shifts of octaethylporphyrin (OEP) are −3.75 ppm (NH) and 10.1 ppm (*meso*-H), respectively. The chemical shifts of these protons depend on the porphyrin ring current and the extent of the porphyrin aggregation.[12] The chemical shifts of the porphyrins **10** are shifted to the higher fields (NH) and the lower fields (*meso*-H) compared with those of OEP. Thus, porphyrins **10** keep a planarity in spite of having sterically hindered structures which prevent the aggregation of porphyrins. The porphyrins **10** provide an interesting framework with bis-pockets at both the sites of porphyrins. Such systems may provide useful models for studying reactions in biological systems such as heme oxygenase.[13] Chemical modification of the porphyrin ring by the direct introduction of sterically hindered groups at both the β and *meso* positions induces distortion of the rings with non-planar porphyrin formation: this has both disadvantages and advantages for the use of such porphyrins as models of biological systems.[14] Since many efficient methods to construct porphyrins starting from pyrrole-2-carboxylates such as **3**, **5** and **7** exist,[4,5] the present pyrrole synthesis provides a useful tool for the construction of porphyrins fused with polycyclic skeletons.

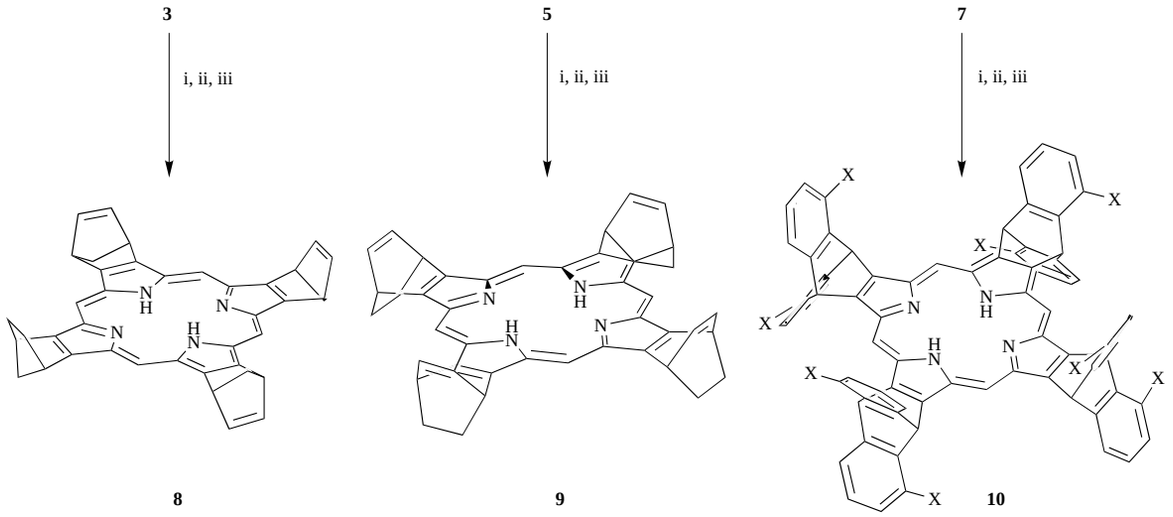
Table 1 Diels–Alder reaction of **1** with substituted anthracenes

X	Reaction conditions	Product **6**	Yield (%)
Cl	Toluene, reflux, 5 h	**6a**	62
CO_2Me	Toluene, reflux, 60 h	**6b**	55
CN	Toluene, reflux, 70 h	**6c**	25
H	Toluene, reflux, 3 h	**6d**	88
Me	Toluene, reflux, 20 h	**6e**	36
Me	Toluene, reflux, 5 h	**6e**	61
OMe	Toluene, reflux, 1.5 h	**6f**	0
OMe	$CHCl_3$, room temp., 18 h	**6f**	82
OCH_2OMe	Toluene, reflux, 1.5 h	**6g**	0
OCH_2OMe	$CHCl_3$, room temp., 120 h	**6g**	65

Table 2 Pyrrole synthesis from the β-nitro sulfones **2**, **4** and **6**: the reaction was carried out at room temperature for 24 h (see Experimental section)

β-Nitro sulfones	Solvent	Base	Product	Yield (%)
2	THF	DBU	**3**	0
2	MeCN	DBU	**3**	61
2	THF	BTPP*	**3**	20
4	THF	DBU	**5**	63
6a	THF	DBU	**7a**	58
6b	THF	DBU	**7b**	81
6c	THF	DBU	**7c**	63
6d	THF	DBU	**7d**	60
6e	THF	DBU	**7e**	90
6f	THF	DBU	**7f**	45
6g	THF	DBU	**7g**	65

* BTPP: *tert*-Butyliminotri(pyrrolidino)phosphorane.



Scheme 2 *Reagents and conditions*: i, $LiAlH_4$, THF, 0 °C, 3 h; ii, *p*-TsOH, $CHCl_3$, room temp., 24 h; iii, *p*-chloranil, $CHCl_3$, room temp., 48 h

Table 3 Absorption and ^{1}H NMR spectra of the porphyrins **8**, **9** and **10** and their Zn complexes

		^{1}H NMR (ppm)	
Porphyrins	λ_{max}/nm	*meso*-H	NH
8	393, 499, 535, 575, 645		
Zn·**8**	405, 534, 571		
9	386, 495, 527, 561, 617	10.40	−4.80
Zn·**9**	400, 527, 561		
10d	395, 501, 532, 570, 623	10.59	−4.92
Zn·**10d**	411, 535, 569		
10e	395, 501, 531, 570, 623	10.52	−4.95
Zn·**10e**	412, 535, 567		

Experimental

Mps were measured with a Yanagimoto BY-1 melting point apparatus. ^{1}H and ^{13}C NMR spectra were recorded on a JEOL-JNM-GSX 270 or JNM-EX 400 spectrometer using tetramethylsilane as an internal standard. IR and UV–visible spectra were obtained with a Hitachi 270-30 and Shimazu UV-2200 spectrometer, respectively. Mass spectra and high resolution mass spectra were measured with a Hitachi M80B spectrometer. FAB mass spectra of porphyrins were measured with a JEOL JMS-DX-300 spectrometer; samples were dissolved in $CHCl_3$ and *m*-nitrobenzyl alcohol was used as a matrix.

Diels–Alder reaction of 1 with dienes

The reaction was carried out according to a literature procedure,[10] where the preparation of **2**, **4** and **6d** are reported. The reaction of **1** with substituted anthracenes was also carried out in a similar way under the reaction conditions shown in Table 1. The adducts, consisting of diastereoisomers except for **6d**, were used directly for the next step without separation of them. All new compounds of the Diels–Alder adducts gave satisfactory spectroscopic data (IR, NMR and Mass).

Compound **6a**: $\delta_H(CDCl_3)$ 4.21 (1 H, m), 5.08 (1 H, m), 5.50 (1 H, d, *J* 2), 5.60 (1 H, d, *J* 2) and 7.05–7.90 (11 H, m); ν_{max}(KBr)/cm^{-1} 1572, 1458, 1362, 1283, 1154, 1084 and 790; *m*/*z* (EI) 460 (M^+).

Compound **6b**: $\delta_H(CDCl_3)$ 3.92, 4.02 (6 H, s, OMe), 4.22 (1 H, m), 5.21 (m, 1 H), 6.30 (1 H, m), 6.57 (1 H, m) and 7.2–8.0 (11 H, m); ν_{max}(KBr)/cm^{-1} 1714, 1556, 1440, 1366, 1312, 1270, 1144 and 760; *m*/*z* (EI) 507 (M^+).

Compound **6c**: $\delta_H(CDCl_3)$ 4.22 (1 H, m), 5.25 (1 H, d, *J* 2), 5.44 (1 H, m), 5.68 (1 H, d, *J* 2) and 7.2–8.1 (11 H, m); ν_{max}(KBr)/cm^{-1} 2223, 1556, 1450, 1364, 1152 and 764; *m*/*z* (EI) 441 (M^+).

Compound **6e**: $\delta_H(CDCl_3)$ 2.28, 2.64 (6 H, s, Me), 4.32 (1 H, m), 5.18 (1 H, m), 5.3–5.4 (2 H, m) and 6.9–7.8 (11 H, m); ν_{max}(KBr)/cm^{-1} 1546, 1470, 1356, 1258, 1152, 1084 and 788; *m*/*z* (EI) 419 (M^+).

Compound **6f**: $\delta_H(CDCl_3)$ 3.85, 3.98 (6 H, s, OMe), 4.22 (1 H, m), 5.08 (1 H, m), 5.22 (1 H, m), 5.40 (1 H, m), 6.9–7.8 (11 H, m); ν_{max}(KBr)/cm^{-1} 1545, 1470, 1360, 1258, 1152; *m*/*z* (EI) 451 (M^+).

Compound **6g**: $\delta_H(CDCl_3)$ 3.48, 3.52, 3.56, 3.58 (6 H, s, OMe), 4.21 (1 H, m), 4.70 (1 H, m), 5.1–5.6 (5 H, m, $CHNO_2$, OCH_2) and 6.8–7.8 (11 H, m); ν_{max}(KBr)/cm^{-1} 1556, 1482, 1364, 1152 and 1052; *m*/*z* (EI) 511 (M^+).

Ethyl 4,7-dihydro-4,7-methano-2*H*-isoindole-1-carboxylate 3

To a stirred solution of **2** (0.28 g, 1.0 mmol) and ethyl isocyanoacetate (0.13 g, 1.0 mmol) in MeCN (10 ml) was added DBU (0.31 g, 2.0 mmol) at 0 °C. The resulting reaction mixture was stirred at room temperature for 24 h after which it was poured into water containing dilute hydrochloric acid. After extraction with ethyl acetate work-up and column chromatography (ethyl acetate–hexane, silica gel) gave **3** (0.12 g, 61%) as colourless needles; mp 96–97 °C; $\delta_H(CDCl_3)$ 1.36 (3 H, t, *J* 7.02, CH_2CH_3), 2.33 and 2.46 (2 H, 2 d, *J* 7.02, 8-H), 3.79 (1 H, m, 4-H), 4.07 (1 H, m, 7-H), 4.29 and 4.30 (2 H, 2 q, *J* 7.02, CH_2CH_3), 6.54 (1 H, d, *J* 1.13, 3-H), 6.75 (2 H, t, *J* 1.84, 5 and 6-H) and 8.01 (1 H, br s, NH); $\delta_C(CDCl_3)$ 14.29 (CH_2CH_3), 44.54 (C-4), 45.25 (C-7), 59.73 (CH_2CH_3), 70.70 (C-8), 113.30, 114.92, 138.60, 142.66 (C-1, 3, 3a, 7a), 143.42 (C-5), 144.66 (C-6) and 161.15 (C=O); ν_{max}(KBr)/cm^{-1} 3308, 2996, 1672, 1410, 1366 and 1106; *m*/*z* (EI) 203 (M^+, 94), 174 (52), 157 (100) and 125 (85) [Found (HRMS): 203.0935. $C_{12}H_{13}NO_2$ requires 203.0946].

Ethyl 4,7-dihydro-4,7-ethano-2*H*-isoindole-1-carboxylate 5

The pyrroles **4** and **7** were prepared in THF by a procedure similar to that adopted for **3**.

Compound **5**: colourless plates; mp 129–130 °C; $\delta_H(CDCl_3)$ 1.37 (3 H, t, *J* 7.02, CH_2CH_3), 1.41–1.67 (4 H, m, 8 and 9-H), 3.87 (1 H, m, 4-H), 4.29 (2 H, q, *J* 7.02, CH_2CH_3), 4.37 (1 H, m, 7-H), 6.50 (2 H, m, 5 and 6-H), 6.57 (1 H, d, *J* 2.13, 3-H) and 8.41 (1 H, br s, NH); $\delta_C(CDCl_3)$ 14.37 (CH_2CH_3), 26.26 (C-9), 26.93 (C-8), 33.10 (C-4), 33.51 (C-7), 59.69 (CH_2CH_3), 112.97, 113.89, 131.11, 136.04 (C-1, 3, 3a, 7a), 135.93 (C-5), 136.39 (C-6) and 161.72 (C=O); ν_{max}(KBr)/cm^{-1} 3328, 2944, 1676, 1428, 1334, 1318, 1148 and 1094; *m*/*z* (EI) 217 (M^+, 16), 189 (100), 172 (13) and 143 (79) (Found: C, 71.78; H, 6.89; N, 6.43. $C_{13}H_{15}NO_2$ requires C, 71.86; H, 6.96; N, 6.44%).

Ethyl 4,9-dihydro-5,10-dichloro-4,9-*o*-benzenonaphtho[2,3-*c*]-pyrrole-1-carboxylate 7a

White powder; mp 195–196 °C; δ_H($CDCl_3$) 1.47 (3 H, t, *J* 7.02, CH_2CH_3), 4.29–4.47 (2 H, m, CH_2CH_3), 5.83 (1 H, s, 4-H), 6.32 (1 H, s, 9-H), 6.75 (1 H, d, *J* 2.75, 3-H), 6.88–6.95 (2 H, m, ArH), 7.02 (2 H, m, ArH), 7.24–7.33 (2 H, m, ArH) and 8.38 (1 H, br s, NH); δ_C($CDCl_3$) 14.45 (CH_2CH_3), 43.88 (C-4), 44.45 (C-9), 60.34 (CH_2CH_3), 114.65, 115.95, 122.17, 122.74, 125.94, 125.99, 126.32, 126.38, 129.18, 129.69, 132.07, 136.23, 143.35, 143.86, 147.50 and 148.23 (1, 3, 3a, 4a, 5, 6, 7, 8, 8a, 9a, 10, 11, 12, 13, 13a) and 161.16 (C=O); ν_{max}(KBr)/cm^{-1} 3308, 1690, 1456, 1424, 1328, 1288 and 1170; *m*/*z* (EI) 383 (M^+, 100%), 348 (32), 302 (51) and 274 (44) (Found: C, 65.62; H, 4.32; N, 3.72. $C_{21}H_{15}NO_2Cl_2$ requires C, 65.64; H, 3.94; N, 3.65%).

Ethyl 4,9-dihydro-5,10-dimethoxycarbonyl-4,9-*o*-benzeno-naphtho[2,3-*c*]pyrrole-1-carboxylate 7b

Pale yellow powder; mp 161–163 °C; δ_H($CDCl_3$) 1.47 (3 H, t, *J* 7.02, CH_2CH_3), 3.96 (3 H, s, 10 CO_2Me), 3.97 (3 H, s, 5 CO_2Me), 4.26–4.40 (2 H, m, CH_2CH_3), 6.75 (1 H, d, *J* 2.75, 3-H), 6.79 (1 H, s, 4-H), 7.00–7.07 (2 H, m, ArH), 7.21 (1 H, s, 9-H), 7.53–7.63 (4 H, m, ArH) and 8.31 (1 H, br s, NH); δ_C($CDCl_3$) 14.47 (CH_2CH_3), 43.36 (C-4), 43.93 (C-9), 51.93 (5 MeO), 51.99 (10 MeO), 60.26 (CH_2CH_3), 114.54, 116.05, 124.87, 124.96, 125.24, 126.12, 126.77, 126.82, 128.04, 128.72, 129.38, 132.74, 136.75, 147.84, 147.93 and 148.94 (1, 3, 3a, 4a, 5, 6, 7, 8, 8a, 9a, 10, 11, 12, 13, 13a), 161.11 (C=O), 167.29 (5 C=O) and 167.52 (10 C=O); ν_{max}(KBr)/cm^{-1} 3320, 1718, 1698, 1292 and 1152; *m*/*z* (EI) 431 (M^+, 100), 407 (31), 372 (21) and 326 (40) [Found (HRMS): 431.1357. $C_{25}H_{21}NO_6$ requires 431.1369].

Ethyl 4,9-dihydro-5,10-dicyano-4,9-*o*-benzenonaphtho[2,3-*c*]-pyrrole-1-carboxylate 7c

Pale yellow powder; mp 241 °C; δ_H($CDCl_3$) 1.53 (3 H, t, *J* 7.02, CH_2CH_3), 4.33–4.51 (2 H, m, CH_2CH_3), 5.83 (1 H, s, 4-H), 6.30 (1 H, s, 9-H), 6.84 (1 H, d, *J* 2.75, 3-H), 7.11–7.18 (2 H, m, ArH), 7.29–7.34 (2 H, m, ArH), 7.60–7.70 (2 H, m, ArH) and 8.67 (1 H, br s, NH); δ_C($CDCl_3$) 14.42 (CH_2CH_3), 45.19 (C-4), 45.76 (C-9), 60.84 (CH_2CH_3), 107.93, 108.54, 115.16, 116.54, 116.94, 117.20, 126.22, 128.00, 128.47, 128.56, 128.64, 130.73, 134.34, 145.97 and 146.66 (1, 3, 3a, 4a, 5, 6, 7, 8, 8a, 9a, 10, 11, 12, 13, 13a), 149.25 (5 CN), 149.77 (10 CN) and 160.93 (C=O); ν_{max}(KBr)/cm^{-1} 3452, 2228, 1556, 1328 and 1152; *m*/*z* (EI) 365 (M^+, 100), 336 (19), 319 (21), 292 (68), 265 (38) and 228 (61) [Found (HRMS): 365.1166. $C_{23}H_{15}N_3O_2$ requires 365.1164].

Ethyl 4,9-dihydro-4,9-*o*-benzenonaphtho[2,3-*c*]pyrrole-1-carboxylate 7d

White powder; mp 186–187 °C; δ_H($CDCl_3$) 1.39 (3 H, t, *J* 7.02, CH_2CH_3), 4.33 (2 H, m, CH_2CH_3), 5.28 (1 H, s, 4-H), 5.78 (1 H, s, 9-H), 6.59 (1 H, d, *J* 2.44, 3-H), 6.86–7.02 (4 H, m, ArH), 7.24–7.39 (4 H, m, ArH) and 8.25 (1 H, br s, NH); δ_C($CDCl_3$) 14.35 (CH_2CH_3), 46.98 (C-4), 47.54 (C-9), 59.91 (CH_2CH_3), 114.10, 115.08, 123.15, 123.69, 124.87, 133.11, 133.25, 145.92 and 146.65 (1, 3, 3a, 4a, 5, 6, 7, 8, 8a, 9a, 10, 11, 12, 13, 13a) and 161.13 (C=O); ν_{max}(KBr)/cm^{-1} 3316, 1694, 1316, 1280, 1132 and 1104; *m*/*z* (EI) 315 (M^+, 100), 269, 241 [Found (HRMS): 315.1265. $C_{21}H_{17}NO_2$ requires 315.1260].

Ethyl 4,9-dihydro-5,10-dimethyl-4,9-*o*-benzenonaphtho[2,3-*c*]-pyrrole-1-carboxylate 7e

Colourless needles; mp 188–190 °C; δ_H($CDCl_3$) 1.44 (2 H, t, *J* 7.01, CH_2CH_3), 2.46 (3 H, s, 5 Me), 2.50 (3 H, s, 10 Me), 4.28–4.44 (2 H, m, CH_2CH_3), 5.53 (1 H, s, 4-H), 6.04 (1 H, s, 9-H), 6.66 (1 H, d, *J* 2.44, 3-H), 6.80–6.89 (4 H, m, ArH), 7.14–7.22 (2 H, m, ArH) and 8.13 (1 H, br s, NH); δ_C($CDCl_3$) 14.54 (CH_2CH_3), 18.47 (5 Me), 18.53 (10 Me), 43.49 (C-4), 44.05 (C-9), 60.03 (CH_2CH_3), 113.86, 115.34, 121.16, 121.78, 124.59, 124.61, 126.69, 126.38, 131.43, 132.03, 133.61, 138.09, 144.55, 145.04, 145.67 and 146.54 (1, 3, 3a, 4a, 5, 6, 7, 8, 8a, 9a, 10, 11, 12, 13, 13a) and 161.25 (C=O); ν_{max}(KBr)/cm^{-1} 3400, 2920, 1696, 1262, 1176, 1092, 1046 and 804; *m*/*z* (EI) 343 (M^+, 100), 298 (19), 282 (33), 254 (25) and 207 (77) [Found (HRMS): 343.1570. $C_{23}H_{21}NO_2$ requires 343.1572. Found: C, 80.34; H, 6.36; N, 3.85. $C_{25}H_{21}NO_6$ requires C, 80.44; H, 6.16; N, 4.08%].

Ethyl 4,9-dihydro-5,10-dimethoxy-4,9-*o*-benzenonaphtho[2,3-*c*]-pyrrole-1-carboxylate 7f

Colourless needles; mp > 250 °C; δ_H($CDCl_3$) 1.44 (3 H, t, *J* 7.02, CH_2CH_3), 3.83 (3 H, s, 5 MeO), 3.84 (3 H, s, 10 MeO), 4.28–4.44 (2 H, m, CH_2CH_3), 5.79 (1 H, s, 4-H), 6.29 (1 H, s, 7-H), 6.58 (1 H, d, *J* 8.24, ArH), 6.59 (1 H, d, *J* 8.24, ArH), 6.68 (1 H, d, *J* 2.13, 3-H), 6.91 (1 H, dd, *J* 8.24, *J* 3.05, ArH), 6.94 (1 H, dd, *J* 8.24, 3.05, ArH), 7.00 (1 H, d, *J* 7.01, ArH), 7.07 (1 H, d, *J* 7.01, ArH) and 8.07 (1 H, br s, NH); δ_C($CDCl_3$) 14.51 (CH_2CH_3), 40.05 (C-4), 40.62 (C-9), 55.64 (5 MeO), 55.92 (10 MeO), 60.00 (CH_2CH_3), 108.48, 108.81, 113.88, 115.44, 116.49, 117.03, 125.79, 125.87, 134.03, 134.22, 134.81, 148.31, 149.02 and 153.96, (1, 3, 3a, 4a, 5, 6, 7, 8, 8a, 9a, 10, 11, 12, 13, 13a) and 154.49 (C=O); ν_{max}(KBr)/cm^{-1} 3416, 1690, 1482, 1266 and 1090; *m*/*z* (EI) 375 (M^+, 100), 344 (23), 330 (11) and 298 (42) [Found (HRMS): 375.1459. $C_{23}H_{21}NO_4$ requires 375.1471].

Ethyl 4,9-dihydro-5,10-dimethoxymethoxy-4,9-*o*-benzeno-naphtho[2,3-*c*]pyrrole-1-carboxylate 7g

Colourless needles, mp 187–188 °C; δ_H($CDCl_3$) 1.41 (3 H, t, *J* 7.01, CH_2CH_3), 3.47 (3 H, s, 5 OCH_2OCH_3), 3.48 (3 H, s, 10 OCH_2OCH_3), 4.31–4.35 (2 H, m, CH_2CH_3), 5.18–5.23 (4 H, m, 5 and 10 OCH_2OCH_3), 5.80 (1 H, s, 4-H), 6.29 (1 H, s, 7-H), 6.62 (1 H, d, *J* 2.13, 3-H), 6.75 (1 H, d, *J* 7.32, ArH), 6.76 (1 H, d, *J* 7.32, ArH), 6.87 (1 H, dd, *J* 7.24, 2.14, ArH), 6.90 (1 H, dd, *J* 7.24, 2.62, ArH), 7.03 (1 H, d, *J* 6.72, ArH), 7.10 (1 H, d, *J* 7.02, ArH) and 8.45 (1 H, br s, NH); δ_C($CDCl_3$) 14.52 (CH_2CH_3), 40.33 (C-4), 40.91 (C-9), 56.00 (5 OCH_2OCH_3), 56.07 (10 OCH_2OCH_3), 60.04 (CH_2CH_3), 94.96 (5 OCH_2OCH_3), 95.03 (10 OCH_2OCH_3), 112.51, 112.75, 114.01, 115.42, 117.63, 118.18, 125.82, 125.84, 133.72, 135.20, 135.78, 138.09, 148.10, 148.90, 151.11 and 151.59 (1, 3, 3a, 4a, 5, 6, 7, 8, 8a, 9a, 10, 11, 12, 13, 13a) and 151.90 (C=O); ν_{max}(KBr)/cm^{-1} 3400, 1700, 1478, 1248, 1152 and 1044; *m*/*z* (EI) 435 (M^+, 100), 390 (19), 358 (20), 330 (83) and 286 (30) [Found (HRMS): 435.1662. $C_{25}H_{25}NO_6$ requires 435.1682].

Synthesis of the porphyrin 10e

To a stirred mixture of $LiAlH_4$ (0.140 g, 3.7 mmol) in THF (5 ml) was added dropwise a solution of the pyrrole **7e** (0.343 g, 1.0 mmol) in THF (10 ml) at 0 °C, and the resulting mixture was stirred at 0–5 °C for 2 h. Excess of $LiAlH_4$ was destroyed by the addition of ethyl acetate after which the mixture was poured into saturated aqueous NH_4Cl and extracted with $CHCl_3$ (100 cm^3 × 3). *p*-TsOH (0.08 g) was added to the combined extracts and the mixture was stirred at room temperature for 24 h. *p*-Chloranil (0.123 g, 0.5 mmol) was added to the reaction mixture which after being stirred at room temperature for 24 h was poured into water. The organic layer was separated, washed with aqueous sodium hydrogencarbonate, dried (Na_2SO_4) and evaporated. The residue was subjected to column chromatography (silica gel, $CHCl_3$) to give **10e** (0.076 g, 27%) as a red powder. Porphyrin **10e** was a mixture of stereoisomers, as demonstrated by a multiplet for the meso protons in its ^1H NMR spectrum: δ_H −4.95 (2 H, NH), 3.0 (24 H, m, Me), 6.94 (8 H, m), 6.98 (16 H, m), 7.42 (8 H, m), 7.75 (8 H, m) and 10.52 (4 H, m, meso-H); λ_{max}/nm ($CHCl_3$) 397, 501, 531, 573 and 636; *m*/*z* (FAB) 1226.57 (M^+) and 1127.57 (100).

Porphyrin 9

The pyrrole **4** gave the porphyrin **9** as a red powder (30%) by a similar procedure to that adopted in the preparation of **10e**. The porphyrin **9** exists as a number of stereoisomers depending

on whether the fused bridgehead groups are *syn* or *anti* to each other; this brings about a complicated set of multiplets in the NMR spectrum for meso or other protons; δ_H −4.80 (2 H, NH), 2.0 (8 H, m), 2.2 (8 H, m), 5.8 (8 H, m), 7.20 (8 H, m) and 10.40 (4 H, m); λ_{max}/nm ($CHCl_3$) 386, 495, 527, 561 and 617; *m*/*z* (EI) 622 (M^+).

Porphyrin 10d

The pyrrole **7d** gave the porphyrin **10d** as a red powder (28%) by a procedure similar to that adopted in the preparation of **10e**; δ_H −4.92 (2 H, NH), 7.03–7.08 (16 H, m), 7.15 (8 H, s), 7.89 (16 H, q, *J* 5.9) and 10.59 (4 H, s); λ_{max}/nm ($CHCl_3$) 395, 501, 531, 570 and 623; *m*/*z* (FAB) 1170.46 (M^+) and 1171.46 (100).

Acknowledgements

This work was supported, in part, by a Grant-in-Aid for Scientific Research (No. 08454203) from the Ministry of Education, Science, Sports and Culture, Japan.

References

1 Recent reviews, see, B. Franck and A. Nonn, *Angew. Chem.*, *Int. Ed. Engl.*, 1995, **34**, 1795; T. D. Lash, *Chem. Eur. J.*, 1996, **2**, 1197, J. L. Seeler and A. K. Burrell, *Top. Curr. Chem.*, 1991, **161**, 177; N. Ono and N. Wada, *J. Synth. Org. Chem. Jpn.*, 1993, **51**, 826; H. Ogoshi and T. Mizutani, *J. Synth. Org. Chem. Jpn.*, 1996, **54**, 906. Some recent papers, see, R. Bonnett and K. A. McManus, *J. Chem. Soc.*, *Chem. Commun.*, 1994, 1219; L. T. Nguyen, M. O. Senge and K. M. Smith, *J. Org. Chem.*, 1996, **61**, 998; C. J. Medforth, M. O. Senge, K. M. Smith, L. D. Sparks and J. A. Shelnut, *J. Am. Chem. Soc*., 1992, **114**, 9859.

2 D. H. R. Barton and S. Z. Zard, *J. Chem. Soc.*, *Chem. Commun.*, 1985, 1098; D. H. R. Barton, J. Kervagoret and S. Z. Zard, *Tetrahedron*, 1990, **46**, 7587; T. D. Lash, J. R. BeBellettini, J. A. Bastian and K. B. Couch, *Synthesis*, 1994, 170; N. Ono, H. Katayama, S. Nishiyama and T. Ogawa, *J. Heterocycl. Chem.*, 1994, **31**, 707; M. Adamczyk and R. E. Reddy, *Tetrahedron Lett.*, 1995, **36**, 7983; E. T. Pelkey, L. Chang and G. W. Gribble, *J. Chem. Soc.*, *Chem. Commun.*, 1996, 1909.

3 N. Ono and K. Maruyama, *Chem. Lett.*, 1988, 1881; N. Ono, H. Kawamura, M. Bougauchi and K. Maruyama, *Tetrahedron*, 1990, **46**, 7483.

4 N. Ono, M. Bougauchi and K. Maruyama, *Tetrahedron Lett.*, 1992, **33**, 1629; Y. Furusho, T. Aida and S. Inoue, *J. Chem. Soc.*, *Chem. Commun.*, 1994, 653; C. Endisch, J. H. Fuhrtop, J. Buschmann, P. Luger and U. Siggel, *J. Am. Chem. Soc.*, 1996, **118**, 6671; K. Czarnecki, L. M. Proniewicz, H. Fujii and J. R. Kincaid, *J. Am. Chem. Soc.*, 1996, **118**, 4680; J. Tang and J. G. Verkade, *J. Org. Chem.*, 1994, **59**, 7793; N. Bag, S.-S. Chern, S.-M. Peng and C. K. Chang, *Tetrahedron Lett.*, 1995, **36**, 6409; K. Ayougou, D. Mandon, J. Fisher, R. Weiss, M. Muther, V. Schunemann, A. X. Trautwein, E. Bill, J. Terner, K. Jayaraj, A. Gold and R. N. Austin, *Chem. Eur. J.*, 1996, **2**, 1159.

5 The synthesis of isoindoles from aromatic nitro compounds was originally reported in 1991, see, K. Maruyama, H. Kawamura and N. Ono, Abstract Chemical Congress of Japan, Yokohama, 1A435, 1991; K. Maruyama and N. Ono, Jpn. Kokai Tokkyo Koho JP 04198168, 1992 (*Chem. Abstr.*, 1993, **118**, 80798*h*); see also, N. Ono, H. Hironaga, K. Simizu, K. Ono, K. Kuwano and T. Ogawa, *J. Chem. Soc.*, *Chem. Commun.*, 1994, 1019.

6 N. Ono, H. Hironaga, K. Ono, S. Kaneko, T. Murashima, T. Ueda, C. Tsukamura and T. Ogawa, *J. Chem. Soc.*, *Perkin Trans. 1*, 1996, 2663; T. D. Lash and B. H. Novak, *Angew. Chem.*, *Int. Ed. Engl.*, 1995, **34**, 683; T. D. Lash and P. Chandrafekar, *J. Am. Chem. Soc.*, 1996, **118**, 8767; T. D. Lash, C. Wijesinghe, A. T. Osuma and J. R. Patel, *Tetrahedron Lett.*, 1997, **38**, 2031.

7 H. Uno, T. Kinoshita, K. Matsumoto, T. Murashima, T. Ogawa and N. Ono, *J. Chem. Res.*, 1996, (*S*), 77; T. Murashima, K. Fujita, K. Ono, K. Kuwano and T. Ogawa and N. Ono, *J. Chem. Soc.*, *Perkin Trans. 1*, 1996, 1403.

8 Recent papers of heterotriptycene: A. Isii, M. Kodachi, J. Nakayama and M. Hoshino, *J. Chem. Soc.*, *Chem. Commun.*, 1991, 751; J. P. Parakka, E. V. Sadanadan and M. P. Cava, *J. Org. Chem.*, 1994, **59**, 4308; T. Kobayashi, H. Suda, H. Takase, R. Irie and H. Kato, *Bull. Chem. Soc. Jpn.*, 1995, **68**, 3269 and references therein.

9 Y. Ramondenc, R. Schwenninger, T. Phan, K. Gruber, C. Kratky and B. Krautler, *Angew. Chem.. Int. Ed. Engl.*, 1994, **33**, 889, in which pyrrole triptycene like **7** was prepared in low yield (33%) by the DIBAH reduction of dinitrile obtained by the Diels–Alder reaction of anthracene with acetylenedicarbonitrile.

10 N. Ono, A. Kamimura and A. Kaji, *J. Org. Chem.*, 1988, **53**, 251.

11 T. Murashima, R. Tamai, K. Fujita, H. Uno and N. Ono, *Tetrahedron Lett.*, 1996, **37**, 8391, in which the effect of solvents and bases on pyrrole formation in the reaction of aromatic nitro compounds with ethyl isocyanoacetate was discussed.

12 C. J. Medforth, C. M. Muzzi, K. M. Shea, K. M. Smith, R. J. Abraham, S. Jia and J. A. Shelnutt, *J. Chem. Soc.*, *Perkin Trans. 2*, 1997, 839 and references therein.

13 C. A. Reed and M. Momenteau, *Chem. Rev.*, 1994, **94**, 659.

14 Many papers deal with distorted non planar porphyrins as models of biological heme, see, K. M. Barkingia, L. Chantrnupomg, K. M. Smith and J. Fajer, *J. Am. Chem. Soc.*, 1988, **110**, 7566; K. M. Barkinga, M. D. Berber, J. Fajor, C. J. Medforth, M. W. Renner and K. M. Smith, *J. Am. Chem. Soc.*, 1990, **112**, 8851; W. Jentzen, M. C. Simpson, J. D. Hobbs, X. Song, T. Ema, N. Y. Nelson, C. D. Medforth, K. M. Smith, M. Veyrat, M. Mazzanti, R. Ramasseul, J. C. Marchon, T. Takeuchi, W. A. Goddard and J. A. Shelnutt, *J. Am. Chem. Soc.*, 1995, **117**, 11 805 and references therein.

Paper 7/04418F
Received 23*rd June* 1997
Accepted 31*st July* 1997